REMARKS

I. Status of the claims

Claims 1-23, 28, 29, and 39-44 are pending in this application. Claims 3, 9, and 41-44 have been withdrawn by the Office for being directed to non-elected subject matter. No claim has been amended in this Response.

II. Rejections under 35 U.S.C. § 103

a. Claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29

The Office rejected claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 under 35 U.S.C. 103(a) as allegedly being unpatentable over US Patent No. 5,411,981 (*Gaillard-Kelly*), in view of US Patent No. 4,946,870 (*Partain*) and the Encyclopedia of Controlled Drug Delivery, (p 307, 309, vol. 1, 1999).

The Office argues that *Gaillard-Kelly* teaches that the compounds of instant formula I have anti-androgenic activity, are useful in dermatology, and can be used with other antiacne components such as retinol or with a product stimulating the growth of hair such as Minoxidil for the treatment of alopecia.

The Office argues that *Partain* teaches a topical film-forming composition for delivering pharmaceutical actives with controlled release and that the pharmaceutical active agents include antiacne agents and anti-alopecia agents. The Office further argues that *Partain* also teaches using solvents including ethanol and glycerin with a chitosan film-forming agent.

According to the Office, "[g]lycerine is a well-known plasticizer in controlled release pharmaceutical art." Office Action at p. 5, citing the Encyclopedia of Controlled Drug Delivery, p. 307, Table 1; p. 309.

The Office concludes that it would have been obvious to one of ordinary skill in the art "to modify the teaching of *Gaillard-Kelly* by formulating a film-forming composition as motivated by *Partain III* because (a) both references teach anti-alopecia compositions; and (b) *Partain* teaches that its film-forming system delivers active agents, including anti-alopecia agents, with constant, controlled rate, and protects the applied area of the skin." Office Action at p. 5; italics added.

Applicants respectfully traverse this rejection. In order to prove a *prima facie* case of obviousness, the Office needs to establish, *inter alia*, that: a) the skilled artisan had motivation to modify the teachings of the prior art; and b) the combined references contain all of the elements of the instant claims. M.P.E.P. § 2143. The Office has failed to meet all of these requirements.

The Office has not provided the requisite motivation to combine the cited references in order to arrive at the claimed invention

The Office has not explicitly discussed how one of ordinary skill in the art would combine the references to meet the recitation of "at least one plasticizer" in independent claims 1, 22, 23, 28, and 29. The Office seems to argue that because *Partain* discloses the optional use of glycerin as diluent or adjuvant in some of *Partain's* compositions, the combination of the references will contain a plasticizer. The Office apparently supports this conclusion by asserting that "[g]lycerine is a well-known plasticizer in controlled release pharmaceutical art."

Even assuming, *arguendo*, that *Partain* and *Gaillard-Kelly* can be combined, the Office has failed to provide the motivation one of ordinary skill in the art would have to specifically use glycerin in a composition according to *Partain* that comprises the

compounds of *Gaillard-Kelly*. "In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." M.P.E.P. § 2143.01.I, internal citation omitted, emphasis added. *Partain* discloses a long list of *optional* diluents and adjuvants, among which glycerin is mentioned. *Partain* at col. 9, lines 58-68; col. 10. lines 16-22. Glycerin in *Partain* is only disclosed as a solvent for chlorpheniramine maleate (an antihistamine; Example 14) and none of the active ingredients used in the treatment of alopecia or acne are dissolved in, or used in conjunction with, glycerin (*see, e.g.*, Examples 15 and 18). The Office has not explained why one of ordinary skill in the art would have been motivated to selectively choose glycerin from among the long list of optional diluents and adjuvants, to be used with the compounds disclosed in *Gaillard-Kelly*.

The "fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish prima facie obviousness." M.P.E.P. § 2143.01.IV. Indeed, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01.III (internal citations omitted, emphasis added). Even if *Partain* and *Gaillard-Kelly* could be combined as argued by the office because both of them disclose compositions useful in the treatment of alopecia or acne, the skilled artisan would not be motivated to employ glycerin with such compositions because *Partain* already discloses compositions for the treatment of alopecia or acne that do not contain glycerin. The Office has not provided any reason

supporting the desirability of having glycerin in the compositions resulting from combining the cited references that would motivate one of ordinary skill in the art to use glycerin in such compositions.

For at least this reason, the Office has not met its burden of proving a *prima facie* case of obviousness and Applicants respectfully request that this rejection be withdrawn.

The combined references fail to teach a composition comprising a plasticizer as instantly claimed

The Office has not explicitly discussed how the combination of the references meets the recitation of "at least one plasticizer" in independent claims 1, 22, 23, 28, and 29. As explained above, Applicants believe that the Office is arguing that the references contain a plasticizer because *Partain* discloses the optional use of glycerin, and the Office believes that glycerin is a plasticizer (stating that "[g]lycerine is a well-known plasticizer in controlled release pharmaceutical art," Office Action at p. 5).

However, contrary to the Office's assertion, glycerin *is not always a plasticizer*. The reference cited by the Office succinctly states that glycerin "has been used as a plasticizer" but fails to indicate the conditions under which such use took place. Encyclopedia of Controlled Drug Delivery, vol 1. at p. 309. The same reference explains that "[p]lasticizers must be compatible, in terms of solubility parameter, with the [control release] polymer to which they are added to make it more flexible. Thus, plasticizers are not general purpose but must be chosen from materials that have been shown to be useful for a particular polymer." *Id.* at p. 307 (underlining added). Notably,

the cited reference does not teach under which circumstances glycerin has been, or could be, used as a plasticizer.

Therefore, even assuming, *arguendo*, that a composition according to *Partain* comprises glycerin and a compound according to *Gaillard-Kelly*, the Office has not showed that glycerin would be acting as a plasticizer in such composition. Because the instant claims comprise "at least one plasticizer," the Office has not shown that the combination of references meets all of the limitations of the claims. "The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." M.P.E.P. § 2142

The mere presence of glycerin as a solvent does not mean that glycerin will impart "suppleness and flexibility" to the composition and therefore act as a plasticizer. *See* specification at p. 9. The rejected claims recite "at least one plasticizer." Therefore, it is the Office's burden to show that even if glycerin is present after the combination of references, glycerin will behave as a plasticizer under the conditions resulting from the combination of references. Thus, because the Office has not shown that, even if combined, the references would produce a composition comprising a plasticizer, the Office has not meet its burden of proving a *prima facie* case of obviousness and Applicants respectfully request that this rejection be withdrawn.

b. Claim 14

The Office rejected claim 14 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23,28, and 29 above, and

"further in view of applicants' disclosure." Office Action at p. 5. Applicants believe the Office meant to say "further in view of US Patent No. 5,916,910 (*Lai*)" rather than "further in view of applicants' disclosure," and will respond to the rejection accordingly. Applicants respectfully traverse this rejection.

The Office admits that the "combined references fail to teach angiotensin converting enzyme inhibitors." Office Action at p. 5. However, the Office argues that "Lai teaches conjugates of dithiocarbamates with pharmacologically active agents, wherein dithiocarbamates are said to reduce cutaneous irritation and alopecia. See col. 3, lines 49-51. Captopril, fosinopril, felopdipine, nicardipine, and nifedipine are taught as pharmaceutical agents. See col. 8, lines 51-54." Office Action at p. 5.

The Office further argues that it would have been obvious to one of ordinary skill in the art "to have modified the teachings of the combined references by adding to the composition captopril as motivated by Lai because all the references are directed to treating alopecia, and Lai teaches captopril are combined with other anti-alopecia agents." *Id.* at p. 5-6.

Contrary to the Office's assertion, *Lai* does not disclose that dithiocarbamates "reduce cutaneous irritation and alopecia." *Lai* discloses conjugates where a dithiocarbamate has been covalently bonded to a pharmacologically active agent. *See, e.g.*, col. 3, lines 61-64. The passage cited by the Office clearly shows that when comparing the advantages of administering a conjugate of dithiocarbamate (DC) *and adriamycin* (an anti-neoplastic agent) *versus administration of adriamycin alone*, the administration of DC-adriamycin reduced irritation and alopecia. *Lai* at col. 3, lines 42-52. Adriamycin is a neo-plastic agent (anti-cancer agent), which has hair loss as a

side effect. *See, e.g.*, section D of the CCO Formulary entry for Adriamycin (2000) (enclosed for the Office's convenience). The passage cited by the Office simply indicates that administering adriamycin conjugated to a dithiocarbamate reduces the hair-loss side effect when compared with the administration of unconjugated adriamycin. *Lai* does not teach that dithiocarbamates reduce hair loss.

Therefore, *Lai* is not directed to treating alopecia and one of ordinary skill in the art would not be motivated to combine *Lai* with the teachings of *Partain* and *Gaillard-Kelly* to arrive at instant claim 14 as suggested by the Office. Even if these references were combined, the result would not be a composition comprising at least one angiotensin converting enzyme inhibitor, which is recited in claim 14.

Additionally, claim 14 depends from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references, at least because the combined references fail to teach a composition comprising a plasticizer. *Lai* was cited only for its disclosure of angiotensins and fails to cure the deficiencies of the other cited references mentioned in section II.a above. Therefore, because claim 14 incorporates the subject matter of claim 1, and claim 1 is not obvious over the cited references, claim 14 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

c. Claim 15

The Office rejected claim 15 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug

Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23,28, and 29 above, and further in view of US Patent No. 5,541,220 (*Ismail*).

The Office admits that *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach methylxanthine compounds. The Office argues, however, that *Ismail* teaches agents for the treatment or protection of the skin and that *Ismail* exemplifies "a capsule that can treat alopecia comprising pentoxifylin, vitamin E, and other ingredients." Office Action at p. 6.

The Office argues that it would have been obvious to one of ordinary skill in the art to add pentoxifylin to the composition of the combined references because *Ismail* and the references are directed to treating alopecia and *Ismail* teaches pentoxifyiline as increasing blood circulation. The Office further argues that the skilled artisan would have been motivated to add pentoxifyline to the composition of the combined references because of the expectation of circulating the active agents of the composition though the body.

Applicants respectfully traverse this rejection. The Office has not provided the motivation one of ordinary skill in the art would have to select pentoxifyline from among the long list of blood-circulation promoters disclosed in *Ismail*. *Ismail* at col. 3, lines 12-27. The Office is respectfully reminded that "[s]ome motivation to select the claimed species or subgenus must be taught by the prior art" when the reference discloses more than one species. *See*, *e.g.*, M.P.E.P. §2144.08(4)(a).

Additionally, claim 15 depends from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references, at least because the combined references fail to teach a composition comprising a plasticizer. *Ismail*

was cited only for its disclosure of pentoxifyline and fails to cure the deficiencies of the other cited references mentioned in section II.a above. Therefore, because claim 15 incorporates the subject matter of claim 1, and claim 1 is not obvious over the cited references, claim 15 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

d. Claims 18 and 19

The Office rejected claims 18 and 19 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 above, and further in view of WO 92/21317.

The Office admits that *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach 2,4-diamino-6-butoxy-3- sulfopyrimidine hydroxide. The Office argues, however, that WO 92/21317 teaches compositions containing a pyridine 1-oxide for combating hair loss and inducing/stimulating hair growth. The Office further argues that the reference "[s]pecifically disclose[s] 2,4-diamino-6-butoxy-3-sulfoxypyridimidine hydroxide." Office Action at p. 7.

The Office argues that it would have been obvious to one of ordinary skill in the art to add the 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition of the combined references because WO 92/21317 and the references are all directed toward combating hair loss. The Office further argues that the "skilled artisan would have been motivated to add 2,4-diamino-6-butoxy-3- sulfopyrimidine hydroxide to the

composition of the combined references because of the expectation of further combating hair loss." *Id.*

Applicants respectfully traverse this rejection. Foremost, Applicants would like to request that the Office identify the page where WO 92/21317 specifically discloses 2,4-diamino-6-butoxy-3- sulfopyrimidine hydroxide because Applicants could not find an explicit recitation of this compound in WO 92/21317. In any event, even if 2,4-diamino-6-butoxy-3- sulfopyrimidine hydroxide is explicitly disclosed, WO 92/21317 also discloses a large number of other compounds useful in the treatment of hair loss and the Office has not provided the motivation one of ordinary skill in the art would have to specifically select 2,4-diamino-6-butoxy-3- sulfopyrimidine hydroxide from among all the compounds disclosed in WO 92/21317. The Office is respectfully reminded that "[s]ome motivation to select the claimed species or subgenus must be taught by the prior art" when the reference discloses more than one species. *See, e.g.*, M.P.E.P. §2144.08(4)(a).

Additionally, claims 18 and 19 depend from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. WO 92/21317 was cited only for its disclosure of pyridine 1-oxide compounds and fails to cure the deficiencies of the other cited references mentioned in section II.a above. Therefore, because claims 18 and 19 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

e. Claims 20 and 21

The Office rejected claims 20-21 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of WO 91/19701.

The Office admits that the combined references fail to teach 2,6-diamino-1,3,5-triazine compounds. Additionally, *the Office failed to provide any support for this rejection.*

All arguments in the Office Action under this subsection are directed to the presence of pyridine 1 oxide compounds in WO 92/21317 (claims 18 and 19), but fail to mention the relevance of WO 91/19701 to the instant rejection. Office Action at p. 7-8.

For at least this reason, the Office has not proved a *prima facie* case of obviousness and Applicants respectfully request that this rejection be withdrawn.

f. Claims 5 and 6

The Office rejected claims 5 and 6 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 as above, and further in view of Cremophor RH 40 Technical Information, 1997 (Cremophor pamphlet).

The Office admits that the combined references fail to teach polyoxyethylene hydrogenated castor oil. The Office argues, however, that the Cremophor pamphlet teaches that "POE hydrogenated castor oil is skin compatible and solubilizes hydrophobic pharmaceuticals including vitamin A (retinoic acid)." Office Action at p. 8.

The Office argues that it would have been obvious to one of ordinary skill in the art "to modify the composition of the combined references by adding to the composition POE hydrogenated castor oil as motivated by [the Cremophor pamphlet] because (a) Gaillard, Partain, and [the Cremophor pamphlet]all teach using retinoic acid; and (b) [the Cremophor pamphlet] teaches that POE hydrogenated castor oil is a well known solubilizer in pharmaceutical/cosmetic art, which solubilizes hydrophobic pharmaceutical agents to form a clear solution." *Id.* The Office further argues that the "skilled artisan would have had a reasonable expectation of successfully producing a stable, clear cosmetic composition comprising retinoic acid and the compound of instant formula (I)." *Id.*

Applicants respectfully traverse this rejection. The Office has not provided the motivation one of ordinary skill in the art would have to substitute the solvent (ethyl alcohol) disclosed in *Partain* to dissolve retinoic acid (*See, e.g.*, Example 15) with cremophor. The Office is respectfully reminded that the "fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish prima facie obviousness." M.P.E.P. § 2143.01.IV. "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01.III (internal citations omitted, emphasis added). *Partain* already

discloses solutions comprising retinoic acid and the Office has not provided the motivation one of ordinary skill in the art would have to substitute cremaphor for the solvent already disclosed in *Partain*, especially since *Partain* has already shown that ethyl alcohol works with the film-forming polymers disclosed therein.

Additionally, claims 5 and 6 depend from claim 1, which as explained in section II.a above, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. The Cremophor pamphlet was cited only for its disclosure of a solvent for retinoic acid and fails to cure the deficiencies of the other cited references mentioned in section II.a above. Therefore, because claims 5 and 6 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 5 and 6 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness and Applicants respectfully request that this rejection be withdrawn.

g. Claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40

The Office rejected claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly* in view of US Patent No. 5,658,559 (*Smith*) and the Encyclopedia of Controlled Drug Delivery.

The Office relies on the Office's previous statements regarding *Gaillard-Kelly* and the Encyclopedia of Controlled Drug Delivery summarized in section II.a above.

The Office argues that *Smith* teaches a film-forming lotion composition that forms a barrier on the surface of the skin to prevent evaporative loss of moisture from the skin. The Office further argues that *Smith* teaches polyvinylpyrrolidone/eicosene copolymers,

polyvinylpyrrolidone/vinyl acetate copolymers, and polyvinylpyrrolidone/hexadecane copolymers as barrier polymers and polysaccharide polymers for time-controlled release of therapeutic agents. The Office states that *Smith's* therapeutic agents include antiacne compounds and that *Smith's* composition "comprises water and polyhydric alcohols such as propylene glycol and glycerol (plasticizer and solvent)." Office Action at p. 9.

The Office concludes that it would have been obvious to one of ordinary skill in the art to modify the teachings of *Gaillard-Kelly* by formulating a topical composition comprising the compound of instant formula (I) in the film-forming lotion of *Smith* "because (a) both references are directed to acne treatment compositions; and (b) Smith teaches that the film-forming formulation provides controlled-release of the actives while protecting the skin and prevent loss of moisture of the skin. The skilled artisan would have had a reasonable expectation of successfully producing a stable and effective film-forming lotion which is useful for treating acne or alopecia." *Id.* at p. 9-10.

Applicants respectfully traverse this rejection. In order to prove a *prima facie* case of obviousness, the Office needs to establish, *inter alia*, that: a) the combined references contain all of the elements of the instant claims and b) the modification would have had a reasonable likelihood of success in light of the prior art. M.P.E.P. § 2143. The Office has failed to meet these two requirements.

The combined references fail to teach a composition comprising a plasticizer as instantly claimed

The Office seems to argue that the recitation "at least one plasticizer" in independent claims 1, 22, 23, 28, and 29 is met by the presence of polyhydric alcohols

(*e.g.*, propylene glycol and glycerin) in the compositions of *Smith.* Office Action at p. 9. However, *Smith* is silent regarding polyhydric alcohols performing the role of plasticizers and further suggests that a polyhydric alcohol is optional in its compositions. *Smith* at col. 2, lines 15-16. The Office seems to be relying again on the Encyclopedia of Controlled Drug Delivery to argue that glycerin is a plasticizer.

However, contrary to the Office's assertion and as explained before, glycerin *is not always a plasticizer.* The reference cited by the Office succinctly states that glycerin "has been used as a plasticizer" but fails to indicate the conditions under which such use took place. Encyclopedia of Controlled Drug Delivery, vol 1. at p. 309. The same reference explains that "[p]lasticizers must be compatible, in terms of solubility parameter, with the [control release] polymer to which they are added to make it more flexible. Thus, plasticizers are not general purpose but must be chosen from materials that have been shown to be useful for a particular polymer." *Id.* at p. 307 (underlining added). Notably, the cited reference does not teach under which circumstances glycerin has been, or could be, used as a plasticizer.

Therefore, even assuming, *arguendo*, that a composition according to *Smith* comprises glycerin and a compound according to *Gaillard-Kelly*, the Office has not showed that glycerin would be acting as a plasticizer in such composition. Because the instant claims comprise "at least one plasticizer," the Office has not shown that the combination of references meets all of the limitations of the claims. "The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." M.P.E.P. § 2142

The mere presence of glycerin as a solvent does not mean that glycerin will impart "suppleness and flexibility" to the film and therefore act as a plasticizer. *See* specification at p. 9. The rejected claims recite "at least one plasticizer." Therefore, it is the Office's burden to show that even if glycerin is present after the combination of references, glycerin will behave as a plasticizer under the conditions resulting from the combination of references. Thus, because the Office has not shown that, even if combined, the references would produce a composition comprising a plasticizer, the Office has not meet its burden of proving a *prima facie* case of obviousness and Applicants respectfully request that this rejection be withdrawn.

Even if glycerin is present in a composition as suggested by the Office, there is no expectation of success that a successful composition would be obtained

The Office has failed to show that one of ordinary skill in the art would have had an expectation of success when combining the cited references to obtain a composition as instantly claimed.

Smith and *Gaillard-Kelly* are completely silent as to the use of a plasticizer in their compositions. The Office apparently cited the Encyclopedia of Controlled Drug Delivery for its disclosure that glycerin "has been used as a plasticizer." Office Action at p. 5. Given that one of ordinary skill in the art would have had no motivation to combine the cited disclosures, there could not be a reasonable expectation of success to arrive at the claimed invention.

Moreover, *Smith* teaches that "[t]he therapeutic agents should be chemically compatible with the other ingredients of the composition (col. 4, lines 47-48), and the instant specification explains that "precipitates of the substances at the application site

after evaporation of the solvent" occurred with conventional aqueous/alcoholic hair lotions. Specification at p. 3, line 25 to p. 4, line 5. Therefore, even if the references were combined, the office has not provided any evidence that one of ordinary skill in the art would have expected that the compounds of *Gaillard-Kelly* would be chemically compatible with the ingredients of the *Smith's* compositions.

For at least these reasons, the Office has not met its burden of proving a prima facie case of obviousness and Applicants respectfully request that this rejection be withdrawn.

III. Conclusions

In view of the foregoing remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Reg. No. 43,911, for

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Carlos M. Tellez
Reg. No. 48,638

Dated: September 26, 2006

Attachments: CCO Formulary entry for Adriamycin (2000) (7 pages)